

CLAIMS

1. An antagonist or an agonist which binds to a strong binding site of CCR5, excluding the compounds described in WO01/40227, WO02/74769 and WO02/74770 and SCH-351125.
2. A preventive and/or therapeutic agent for an allergic disease, an inflammatory disease, an immune disease and/or a cancer, which comprises the antagonist or the agonist according to claim 1.
3. The preventive and/or therapeutic agent according to claim 2, wherein the allergic disease, the inflammatory disease, the immune disease and the cancer are diseases selected from asthma, atopic dermatitis, nettle rash, allergic bronchopulmonary aspergillosis, allergic eosinophilic gastroenteritis, nephritis, nephropathy, hepatitis, arthritis, rheumatoid arthritis, psoriasis, rhinitis, conjunctivitis, ischemia-reperfusion injury, multiple sclerosis, ulcerative colitis, acute respiratory distress syndrome, shock accompanied by bacterial infection, diabetes mellitus, autoimmune disease, transplanted organ rejection reaction, immunosuppression, cancer metastasis, HIV infection and acquired immunodeficiency syndrome.
4. The preventive and/or therapeutic agent according to claim 2, wherein the immune disease is HIV infection, acquired immunodeficiency syndrome and/or transplanted organ rejection reaction.
5. A method for screening a compound which binds to a strong binding site of CCR5, which comprises

- (a) allowing a CCR5 expressing cell or a membrane fraction thereof to contact with a compound to be tested,
- (b) washing the cell or the membrane from 1 to 12 times, and
- (c) adding a labeled ligand and measuring amount of the bound labeled ligand.

6. The method according to claim 5, wherein the cell or the membrane is washed from 6 to 10 times.

7. A method for screening a compound which binds to a strong binding site of CCR5, which comprises

- (a) allowing a CCR5 expressing cell or a membrane fraction thereof to contact with a compound to be tested,
- (b) allowing the test compound-bound cell or a membrane fraction thereof prepared in the above (a) to contact with a labeled anti-CCR5 antibody, and
- (c) measuring the labeled anti-CCR5 antibody bound to the CCR5 expressing cell or a membrane fraction thereof.

8. The method according to claim 7, wherein the anti-CCR5 antibody is 45531.111 antibody and/or 45523.111 antibody.

9. A method for measuring an occupying ratio of a compound bound to a CCR5 expressing cell or a membrane fraction thereof, which comprises

- (a) allowing a CCR5 expressing cell or a membrane fraction thereof to contact with a compound to be tested,
- (b) allowing the test compound-bound cell or a membrane fraction thereof prepared in the above step (a) to contact with a labeled anti-CCR5 antibody, and

(c) calculating an occupying ratio of the compound bound to CCR5 on the cell or membrane fraction thereof, based on the ratio of a bound amount of the anti-CCR5 antibody when the compound is bound to CCR5 to a bound amount of the anti-CCR5 antibody when the compound is not bound to CCR5, which is defined as 100%.

10. A method for periodically monitoring an occupying ratio of a compound which binds to a binding site on a CCR5 expressing cell in blood, which comprises

(a) administering a compound which binds to a binding site of CCR5 to a mammal and then separating a cell population containing a cell expressing CCR5 in blood,

(b) allowing the separated cell population to contact with a labeled anti-CCR5 antibody, and

(c) calculating an occupying ratio of the compound which binds to a binding site of CCR5 on the separated cell, based on the ratio of a bound amount of the anti-CCR5 antibody when the compound is bound to CCR5 to a bound amount of the anti-CCR5 antibody when the compound is not bound to CCR5, which is defined as 100%.

11. The method according to claim 10, wherein the anti-CCR5 antibody is 45531.111 antibody and/or 45523.111 antibody.

12. A method for determining a dose and an administration frequency which show such an efficacy that an inhibition ratio of about 50% or 90% can be obtained in administering a compound which binds to a binding site of CCR5, which comprises:

(a) measuring IC50 value or IC90 value of the inhibitory activity of a compound which binds to a binding site of CCR5, by an in vitro activity measuring method,

- (b) calculating an occupying ratio of a compound which binds to a binding site of CCR5 on a CCR5 expressing cell at a compound concentration corresponding to the IC50 value or IC90 value described in the above (a), by the method according to claim 9, and
- (c) comparing the occupying ratio of a compound which binds to a binding site of CCR5, obtained at each dose and monitoring time by the monitoring method according to claim 10, with the occupying ratio obtained by the method described in the above (b).

13. The method according to claim 12, wherein the in vitro activity measuring method is an anti-HIV activity measuring method.

14. A preventive and/or therapeutic agent for an allergic disease, an inflammatory disease, an immune disease and/or a cancer, which comprises a compound which binds to a strong binding site of CCR5 selected by the method according to any one of claim 5, 7, 9, 10 and 12 as an active ingredient.

15. The preventive and/or therapeutic agent according to claim 14, wherein the immune disease is HIV infection, acquired immunodeficiency syndrome and/or transplanted organ rejection reaction.

16. The preventive and/or therapeutic agent according to claim 2 or 14, wherein the administration method is to administer it orally or parenterally at intervals of one day, two days, three days or several days.

17. The preventive and/or therapeutic agent according to claim 16, wherein the immune disease is HIV infection, acquired immunodeficiency syndrome and/or transplanted organ rejection reaction.

18. A method for screening an antagonist or an agonist which binds to a strong binding site of CCR5, which comprises administering it orally or parenterally at intervals of one day, two days, three days or several days.

19. An antagonist or an agonist which binds to a strong binding site of a chemokine receptor.

20. A preventive and/or therapeutic agent for an allergic disease, an inflammatory disease, an immune disease and/or a cancer, which comprises the antagonist or the agonist according to claim 19.

21. The preventive and/or therapeutic agent according to claim 20, wherein the allergic disease, inflammatory disease, immune disease and cancer are diseases selected from asthma, atopic dermatitis, nettle rash, allergic bronchopulmonary aspergillosis, allergic eosinophilic gastroenteritis, nephritis, nephropathy, hepatitis, arthritis, rheumatoid arthritis, psoriasis, rhinitis, conjunctivitis, ischemia-reperfusion injury, multiple sclerosis, ulcerative colitis, acute respiratory distress syndrome, shock accompanied by bacterial infection, diabetes mellitus, autoimmune disease, transplanted organ rejection reaction, immunosuppression, cancer metastasis, HIV infection and acquired immunodeficiency syndrome.

22. A method for screening a compound which binds to a strong binding site of a chemokine receptor, which comprises

- (a) allowing a chemokine receptor expressing cell or a membrane fraction thereof to contact with a compound to be tested,
- (b) washing the cell or the membrane from 1 to 12 times, and
- (c) adding a labeled ligand and measuring an amount of the bound labeled ligand.

23. A method for screening a compound which binds to a strong binding site of a chemokine receptor, which comprises

- (a) allowing a chemokine receptor expressing cell or a membrane fraction thereof to contact with a compound to be tested,
- (b) allowing the test compound-bound cell or a membrane fraction thereof prepared in the above step (a) to contact with a labeled anti-chemokine receptor antibody, and
- (c) measuring the labeled anti-chemokine receptor antibody bound to the chemokine receptor expressing cell or a membrane fraction thereof.

24. A preventive and/or therapeutic agent for an allergic disease, an inflammatory disease, an immune disease and/or a cancer, which comprises a compound which binds to a strong binding site of a chemokine receptor selected by the method according to claim 22 or 23 as an active ingredient.

25. A method for preventing and/or treating a CCR5 intervening disease in a mammal, which comprises administering an effective amount of the agonist or the antagonist according to claim 1.

26. A method for preventing and/or treating a chemokine receptor intervening disease in a mammal, which comprises administering an effective amount of the antagonist or the agonist according to claim 19.

27. A method for preventing and/or treating an allergic disease, an inflammatory disease, an immune disease and/or a cancer, which comprises administering a compound which binds to a strong binding site of CCR5 selected by the method according to any one of claims 5, 7, 9, 10 and 12 as an active ingredient.

28. Use of the agonist and/or the antagonist according to claim 1 for producing a preventive and/or therapeutic agent for a CCR5 intervening disease.

29. Use of the agonist and/or the antagonist according to claim 19 for producing a preventive and/or therapeutic agent for a chemokine receptor intervening disease.

30. Use of a compound which binds to a strong binding site of CCR5, which is selected by the method according to any one of claims 5, 7, 9, 10 and 12, for producing a preventive and/or therapeutic agent for a CCR5 intervening disease.